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(21) International Application Number: PCT/GB98/03137 (22) International Filing Date: 21 October 1998 (21.10.98) (30) Priority Data: 9722448.9 23 October 1997 (23.10.97) GB (71) Applicant (for all designated States except US): AKZO NOBEL UK PLC [GB/GB]; 50 George Street, London W1A 2BB (GB). (72) Inventor; and (75) Inventor/Applicant (for US only): COX, Roland [GB/GB]; 11 Wickersley Close, Darley Abbey, Derby DE22 2XT (GB). (74) Agent: HALE, Stephen, Geoffrey; J.Y. & G.W. Johnson, Kingsbourne House, 229-231 High Holborn, London WC1V 7DP (GB).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: METHODS OF CONTROLLING HOUSE DUST MITES AND BEDMITES (57) Abstract Polymeric articles such as fibres and foams having incorporated therein a chemical compound which has antifungal activity against fungi of the groups <i>Aspergillus glaucus</i> and/or <i>A. restrictus</i> are useful in controlling house dust mites and bedmites <i>Dermatophagoides spp.</i>		

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METHODS OF CONTROLLING HOUSE DUST MITES AND BEDMITESField of the invention

This invention relates to methods of controlling house dust mites and bedmites (hereinafter HDM). HDM are typically 5 Dermatophagoides spp., one species of particular significance being D. pteronyssinus.

A major food source for HDM is dead skin fragments (dander). Such fragments are continually shed by humans in considerable quantities. HDM proliferate in particular in 10 bedding, including the fillings of pillows and mattresses, and in upholstered articles and fibrous floor coverings. HDM are xerophilic organisms which do not require liquid water, and they live in the absence thereof. They demand a high humidity environment, requiring a relative humidity (R.H.) 15 of about 70 to 80 percent to survive. They absorb little water from the atmosphere and are effectively reliant on their food as the source of water. HDM typically excrete about 20 dung pellets per day. These pellets are very dry and brittle and are about 30 micron in size. They are 20 readily broken up into particles about 1-10 micron in size. In the absence of free moisture, these particles readily acquire a positive static charge and become airborne. They are of respirable size and are accordingly able to enter the bronchial tubes of the human lung, where they become 25 deposited on the mucus layer in the tubes and absorb water. The particles contain toxins, which are released when the particle is hydrated, and they can cause rapid allergic reactions, including bronchial inflammation and asthmatic symptoms. One such allergenic toxin of major importance is 30 Der p I, which is a highly-stable water-soluble glycopeptide of molecular weight 30,000 derived from the digestive system of D. pteronyssinus.

Considerable effort has been expended in devising methods for controlling allergic reactions caused by the 35 presence of HDM. One general method is the topical use of

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acaricides (the generic name for substances lethal to mites). Other methods rely upon control of the allergenic particles, for example by encasing them or by denaturing or destroying the allergens they contain. A further method
5 relies on the topical application of fungicides. Dead skin fragments as shed have a very low moisture content and a high fat content. As such, they are a poor food source for HDM. Furthermore, HDM require a source of B-group vitamins. Certain microscopic fungi which thrive in the
10 absence of liquid water (xerophilic fungi) grow on dead skin fragments, and they have the ability to absorb moisture from the atmosphere. In consequence, the moisture content of the fragments is raised; their fat content is reduced; and furthermore B-group vitamins and ergosterol, a precursor of
15 vitamin D, are generated. All this makes the fragments a more suitable food source for HDM. Many such fungi belong to the Aspergillus glaucus and A. restrictus groups. Particular species include A. penicilloides and Eurotium repens (A. repens).

20 It is believed that Aspergillus spp. such as A. repens and A. penicilloides are not responsible per se for allergic reactions in humans of the kind induced by HDM.

Topical application of fungicides has the disadvantage that repeated treatment at regular intervals is required for
25 continued control of HDM. Furthermore, fungicides are inherently toxic materials, and domestic topical application of such substances has been criticised for that reason. It is an object of the invention to provide a means of overcoming these disadvantages.

30 Disclosure of the invention

According to the invention, there is provided in a first aspect the use of a polymeric article having incorporated therein a chemical compound which has antifungal activity against fungi of the groups Aspergillus
35 glaucus and/or A. restrictus as a means of controlling HDM.

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Particular species of such fungi include A. penicilloides and A. repens. A particular species of HDM is D. pteronyssinus. The chemical compound may exhibit fungicidal and/or fungistatic activity.

5 The polymeric article may be a natural article, for example a cellulosic fibre, into which the chemical compound has been incorporated by, for example, a dyeing process. Alternatively, which may be preferred, the polymeric article may be a manmade article such as a fibre or foam into which
10 the chemical compound has been incorporated by a dyeing process or, more preferably, during the course of its manufacture. In the case of a fibre, such a manmade article may be of a natural polymer such as cellulose or of a synthetic polymer such as an acrylic polymer based on
15 polyacrylonitrile. Manmade fibres are described, for example, in a series of articles entitled "Fibers" in Ullmann's Encyclopaedia of Industrial Chemistry, 5th edition (VCH Publishing), Vol. A10 (1987) and A11 (1988). In the case of a foam, the manmade article may be of a synthetic
20 polymer such as a polyurethane. Fibres are used for the manufacture of textile articles such as bedding fabrics (including sheets, blankets, pillowcases, mattress covers and the like), upholstery fabrics and floor coverings (carpets). Both fibres and foams are used as filling
25 materials in articles such as pillows, mattresses, duvets and cushions, in which dander may accumulate and HDM thrive. Foams are used as backing materials and underlays for carpets.

 According to the invention there is provided in a
30 second aspect a filling material for an article of bedding or an upholstered article, characterised in that in said filling material is incorporated a chemical compound which exhibits antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus. The filling
35 material is preferably in fibrous form. The invention further provides an article of bedding or an upholstered article filled with such material. The invention further

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provides a carpeting material which includes a fibre or foam incorporating such a chemical compound.

Insects such as HDM and mammals such as humans on the one hand and fungi such as Aspergillus spp. on the other hand belong to different taxonomic kingdoms. Many substances are known which are toxic to organisms within one kingdom but are effectively non-toxic to organisms within other kingdoms. The same is true, although to increasingly lesser degrees, between the lower taxonomic divisions beginning with phyla, classes and orders. It is an advantage of the invention that it can make use of antifungal compounds having low toxicity to higher mammals including humans and domestic animals and to other domestic pet creatures. The use of such compounds is accordingly preferred.

Acrylic fibres which incorporate neutral organic fungicidal compounds such as tolnaftate (which is a preferred compound), bifonazole, clotrimazole, miconazole, dichlorophene or hexachlorophene are disclosed in GB-A-2,309,461, and these fibres may be preferred in the invention. Another suitable compound is triclosan. The amount of the fungicidal compound in such fibres is preferably in the range from 0.01 to 2 percent by weight on the weight of fibre. Similar amounts of such fungicidal compounds are suitable also in other kinds of polymeric article of the invention.

Incorporation of the antifungal compound within the polymeric article has the advantages that release of the compound into the environment is minimised and that the antifungal effect is long-lasting and endures throughout laundering and dry-cleaning. Wet-spun acrylic fibres may have the advantage of a fissured structure, which both confers good moisture transport properties and assists diffusion of the antifungal compound to the fibre surface following depletion therefrom. The low moisture regain of synthetic fibres such as acrylic fibres may also be

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advantageous in maintaining a low humidity environment and thereby interfering with growth of Aspergillus spp. and HDM.

The invention is illustrated by the following Example, in which parts and proportions are by weight unless
5 otherwise specified:-

Example

This Example illustrates the fungicidal activity against A. repens of acrylic fibres which incorporate a fungicide and of the use of such fibres in controlling HDM.

10 Acrylic fibres containing 0.4% tolnaftate were prepared by a similar method to that disclosed in Example 1 of GB-A-2,309,461. Such fibres are available commercially from Courtaulds Fibres (Holdings) Limited under the Trade Mark AMICOR AF. Acrylic fibres containing no antifungal agent
15 (available from Courtaulds Fibres (Holdings) Limited under the Trade Mark COURTELLE) were used as control. The antimicrobial activity of the fibres was measured by the parallel streak method disclosed in Example 1 of GB-A-2,309,461, but using a culture of A. repens (IMI
20 094150) containing ca. 3×10^6 spores/ml. Test plates were incubated at 25°C for 4 days. The widths of inhibition zones of fungal growth were measured, and the results (overall range and in parenthesis the average of 12 measurements) are reported in the Table below:

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Table 1

Width of inhibition zone

Control	Confluent growth in all streaks on all plates	
	Minimum mm	Maximum mm
5 Fibre with tolnaftate	0-2 (0.7)	2-6 (3.9)

Human skin (provided by a chiropodist) was sterilised, ground into fine fragments and wetted with synthetic perspiration. It was then used as a culture medium for A. repens. A needle punched nonwoven fabric of open structure
 10 was placed in a deep glass dish, to which was then added a known amount of the A. repens culture and fifty HDM. Sticky tape was affixed to the upper part of the dish wall to entrap HDM attempting to climb the wall. The dish was then cultured for eight weeks at room temperature and 75% R.H.
 15 The number of HDM stuck to the tape was recorded. Live HDM associated with the fabric were driven out by application of heat, and their number was recorded. The results shown in Table 2 were obtained (average of three cultures in each case).

20

Table 2

Fabric	HDM on tape	HDM with fabric	Total
Amicor AF	36.6	16.0	42.6
Amicor AB	21.7	1.3	23.0
50/50 Amicor AF/Amicor AB	11.3	2.3	13.6
25 Courtelle	32.3	46.0	78.3

AMICOR AB (Trade Mark of Courtaulds Fibres (Holdings) Limited) is an acrylic fibre containing triclosan made in similar manner to AMICOR AF.

The average number of HDM associated with the Amicor AF
 30 fabric may be distorted by an apparent rogue result; the individual numbers recorded were 4, 9 and 35.

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If a large number of HDM is found associated with the fabric, the presence of HDM on the tape suggests a thriving culture which is attempting to colonise other areas. If a small number of HDM is found associated with the fabric, the presence of HDM on the tape suggests an attempt by HDM to emigrate from a barren environment.

In comparative experiments, the same procedure was followed except that a synthetic food medium for HDM was used instead of the A. repens culture. HDM thrived on all the samples, and there was no significant difference in HDM numbers between any of the samples.

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CLAIMS

1. The use of a polymeric article having incorporated therein a chemical compound which has antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus as a means of controlling house dust mites and bedmites.
2. The use according to claim 1, wherein the polymeric article is a fibre.
3. The use according to claim 2, wherein the fibre is
10 a manmade fibre into which the chemical compound was incorporated during the course of its manufacture.
4. The use according to claim 3, wherein the fibre is an acrylic fibre.
5. The use according to any one of claims 2 to 4,
15 wherein the fibre is incorporated in a textile article.
6. The use according to claim 5, wherein the textile article is a bedding fabric.
7. The use according to claim 1, wherein the polymeric article is a foam.
- 20 8. A filling material for an article of bedding or an upholstered article, characterised in that in said filling material is incorporated a compound which exhibits antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus.
- 25 9. An article of bedding or upholstered article, characterised in that it is filled with a filling material according to claim 8.

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10. A bedding fabric, characterised in that it comprises fibre having incorporated therein a chemical compound which has antifungal activity against fungi of the groups Aspergillus glaucus and/or A. restrictus.

INTERNATIONAL SEARCH REPORT

Inter. Appl. No.

PCT/GB 98/03137

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 A01N25/34 D06M16/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A01N D06M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 24484 A (SOGILO NV ;KLUFT PETER CORNELIS SIEGFRIED (BE)) 10 July 1997 see claims see page 4, paragraph 3 ---	1-10
Y	EP 0 047 553 A (GIST BROCADES NV) 17 March 1982 see page 2, line 11 - line 28 ---	1-10
Y	GB 2 309 461 A (COURTAULDS FIBRES) 30 July 1997 cited in the application see claim 13 -----	1-10

☐ Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

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Information on patent family members

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